




Green Engineering and Sustainability for the Pharmaceutical Industry:

Government Programs and Partnerships

November 18, 2008



Government Programs and Partnerships

- Introduction to Green Engineering: Nhan Nguyen, EPA (10 minutes)
- Green Chemistry and Green Engineering Tools: Richard Engler, Sharon Austin, EPA: (10 minutes)
- GlaxoSmithKline (GSK)/North Carolina State University (NCSU), Partial Life Cycle Modules: Conchita Jiménez-González, GSK (10 minutes)
- Green Pharma: Maryann Helferty, EPA Region 3: (10 minutes)
- NIST MEP Programs on By-Product Synergies and Emerging 3rd Party Markets for Recovered Solvent Waste: Carroll Thomas, Department of Commerce / NIST / MEP: (10 minutes)
- Promoting Environmental Stewardship through Industry/ Government Collaborative Partnerships: Carlos Ramos, EPA Region 2 (15 minutes)
- Initiatives on energy management and Green Engineering at Pharmaceutical Operations in Puerto Rico, Eduardo Cordero (Pfizer) (20 – 30 minutes)
-  Recap/Putting the Pieces Together: Sharon Austin (20 minutes)

Q&A to Entire Panel at end of Session

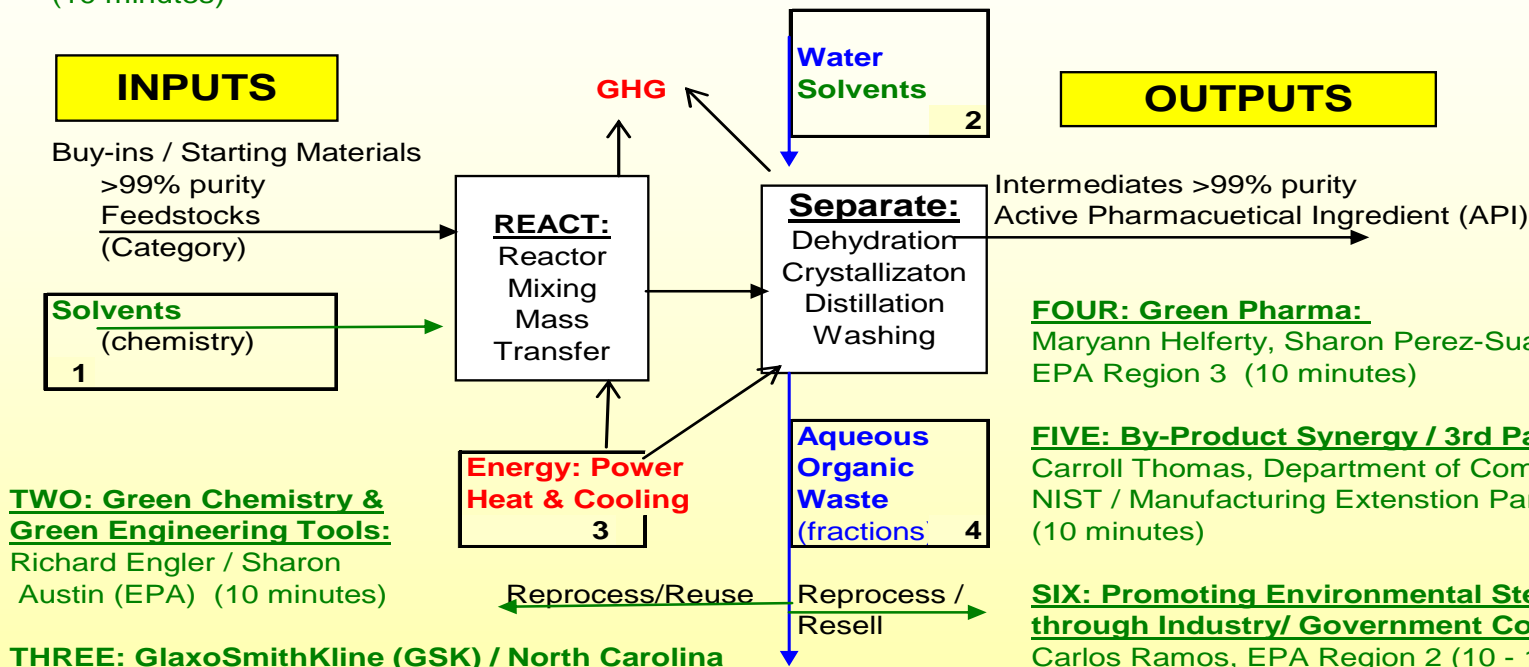
Session Overview

GE and Sustainability in Pharmaceutical Industry - Government Programs and Partnerships

Tuesday, November 18, 2008 3:15 - 5:30, Convention Center 106-A

ONE: Introduction to Session and Green Engineering (GE): Nhan Nguyen, EPA

(10 minutes)



TWO: Green Chemistry & Green Engineering Tools:

Richard Engler / Sharon Austin (EPA) (10 minutes)

THREE: GlaxoSmithKline (GSK) / North Carolina State University (NCSTU), Partial Life Cycle Modules:

Conchita Jiménez-González, David Constable, GSK (10 minutes)

Recap: Putting the Pieces Together

Sharon Austin (20 minutes)

FOUR: Green Pharma:

Maryann Helferty, Sharon Perez-Suarez, EPA Region 3 (10 minutes)

FIVE: By-Product Synergy / 3rd Party Markets

Carroll Thomas, Department of Commerce (DOC) / NIST / Manufacturing Extension Partnership (MEP) (10 minutes)

SIX: Promoting Environmental Stewardship through Industry/ Government Collaborations

Carlos Ramos, EPA Region 2 (10 - 15 minutes)

SEVEN: Initiatives on energy management and Green Engineering at Pharmaceutical Operations in Puerto Rico

Eduardo Cordero (Pfizer) (20 - 30 minutes)

Q&A: End of sessions to all presenters. Panel Composition:

Constable, Gonzalez (GSK) Cordero (Pfizer) Nguyen, Engler, Austin, Helferty, Perez-Suarez, Ramos (EPA) & Thomas (DOC)



Introduction to Green Engineering

Nhan Nguyen
EPA Green Engineering Program

November 18, 2008



What Is Green Engineering?

- **The ADAPTATION, design, commercialization and use of processes and products that are technically and economically feasible while minimizing:**
 - **Generation of pollution at the source**
 - **Risk to human health and the environment**



Green Engineering Goals and Activities

- Drive towards sustainability
- Systematic tiered assessment process
- Create awareness and innovative use of resources and technologies already currently available

Which will...

*... Dispel the myth that
environmental projects cost money*



Program Background

- Pollution Prevention Act 1990
- Green Chemistry initiated in 1991 & 1992
- First GE work started in 1994 to support New Chemicals Program
- Research indicated little expertise in environmental risk in academic and industry, or standardized courses on pollution prevention
- Input from academic & industry at AIChE March 1998 (New Orleans)
- GE Program officially started in 1998



Green Engineering Education

- GE Textbook



- GE Modules

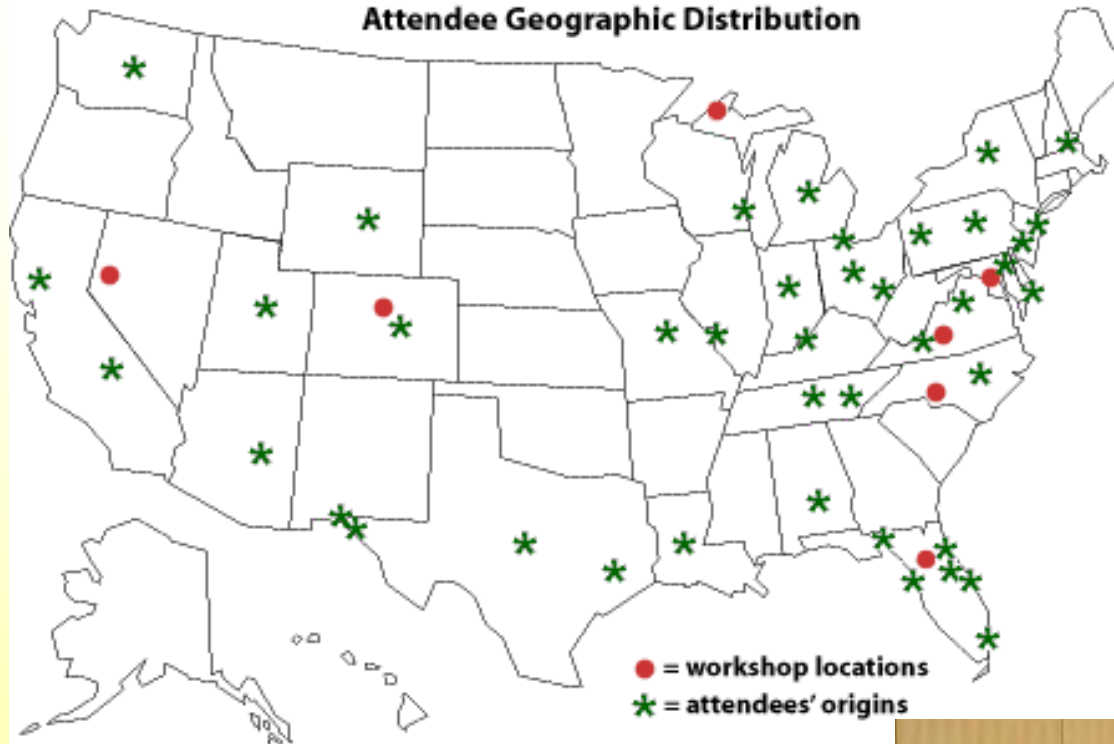


- Educator Workshops



Green Engineering Workshops

Green Engineering Workshops
Attendee Geographic Distribution



Green Engineering Materials

- Environmental Literacy – Speak the same language
- Get the tools to measure, evaluate and set standards from the micro to macro

THEN YOU ARE ABLE TO
Move Beyond the Plant Boundary
(LCA DfE & Industrial Ecology)



Leveraging Activities with Academia and Bridging Activities with Industry

Academia

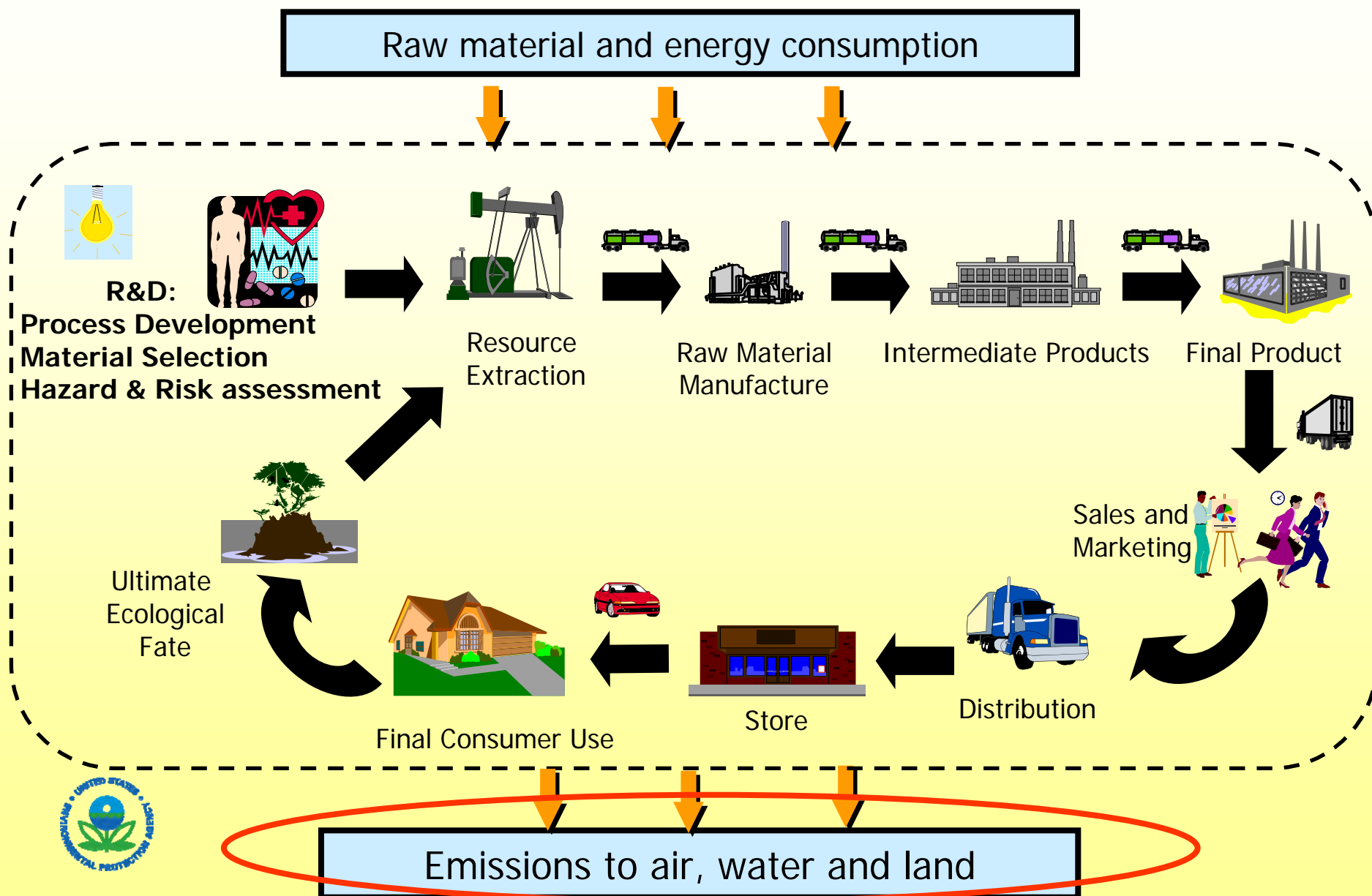
- Center for Sustainable Engineering
- Compilation of materials termed Sustainability Science and Engineering Education (SSEE) materials
- Grant submitted to NSF June 2004 for BookBuild populated with SSEE materials
- Grant awarded January 2005

Industry

- Refineries and paper industry
- Partnership with pharmaceutical industry
- Pilot project in Puerto Rico

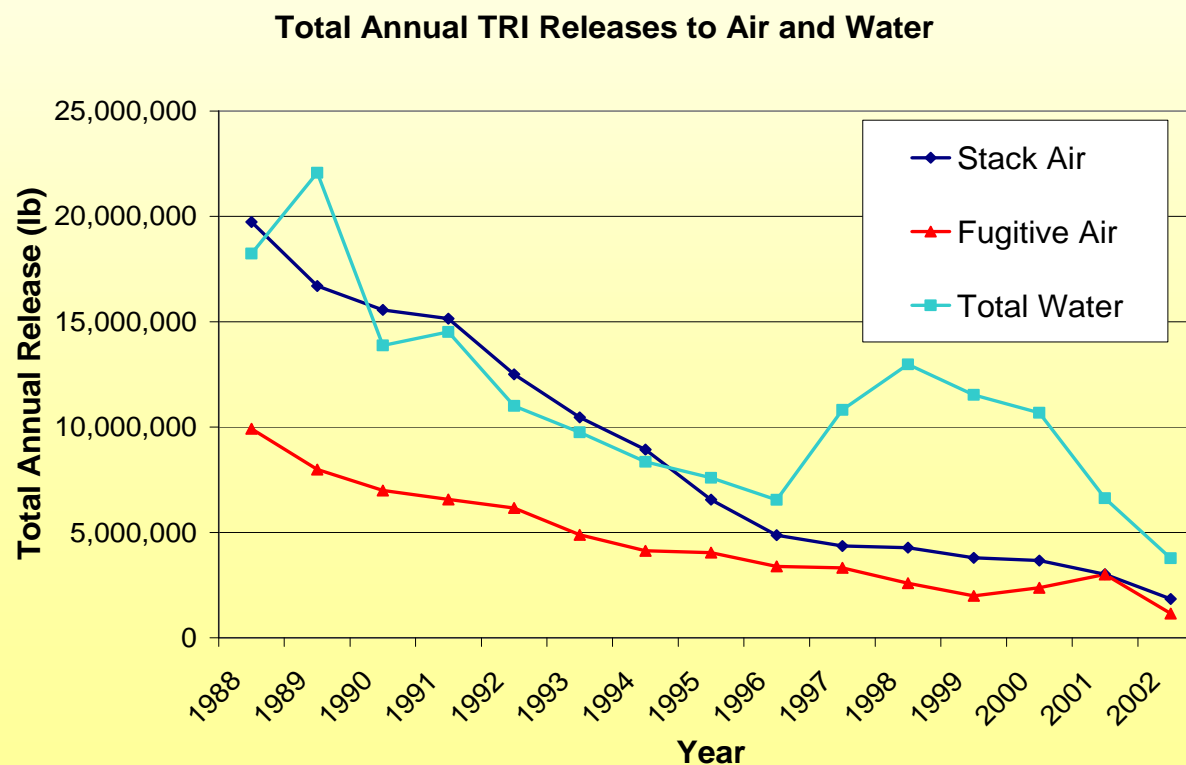


Life Cycle Assessment – The very big picture



Pharmaceutical Environmental Footprint and Progress

- Success 1998 to 2002
 - 91% decrease in stack air releases
 - 88% decrease in fugitive air releases
 - 79% decrease in water releases



More To Do...

- On average 1 kg API generates 99 kg waste
- Reaction concentrations: 15% reactants and 85% solvents
- Lack of solvent recovery for reuse or resale to 3rd party markets
- Wasted energy and lost opportunities



What About FDA?

- Understand need to maintain purity profiles
- Post-process opportunities
- FDA movement away from process spec to product spec
- Changes to manufacturing/purity profile that do not change product quality should not need to involve FDA

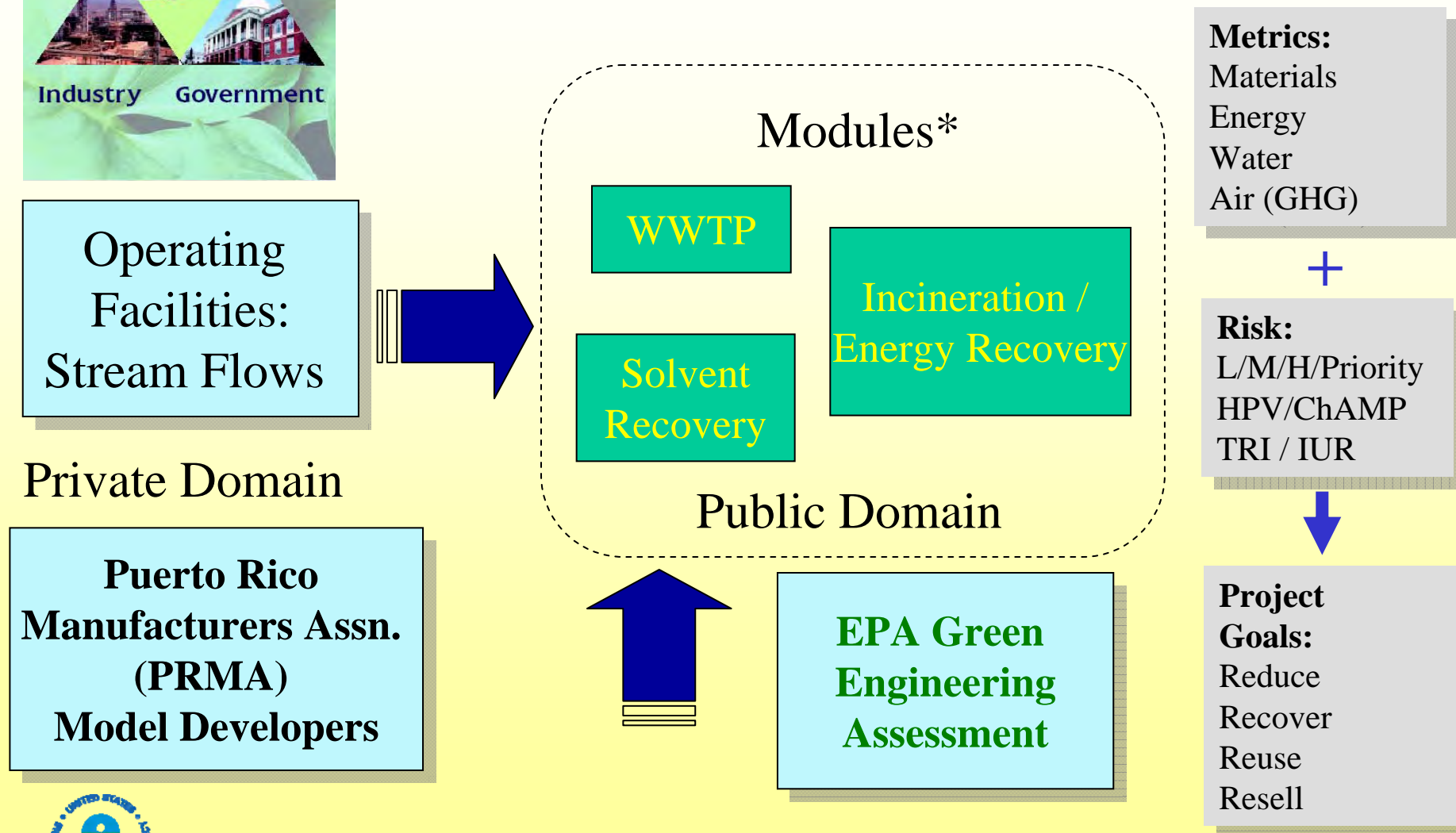


Academia



Industry Government

Material Flow to Metrics



*Jimenez-Gonzalez C, Overcash MR and Curzons AD. J. Chem. Technol. Biotechnol. 71:707-716 (2001)

Pilot Expansion: National Stewardship Challenge

- Case study approach
- Expand best practices to sector
- EPA HQ, EPA regions, states, industry partnership
- EPA P2 grants
- Workshops at industrial clusters
- Technology transfer



Contact Information

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Green Chemistry and Green Engineering Tools

**Rich Engler
EPA Green Chemistry Program**

**Sharon Austin,
EPA Green Engineering Program**

November 18, 2008



Contact Information

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Program
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Green Engineering Tools

- **EPI Suite**

- Physical/chemical property and environmental fate estimation models
- Screening level tool
- <http://www.epa.gov/oppt/exposure/pubs/episuite.htm>



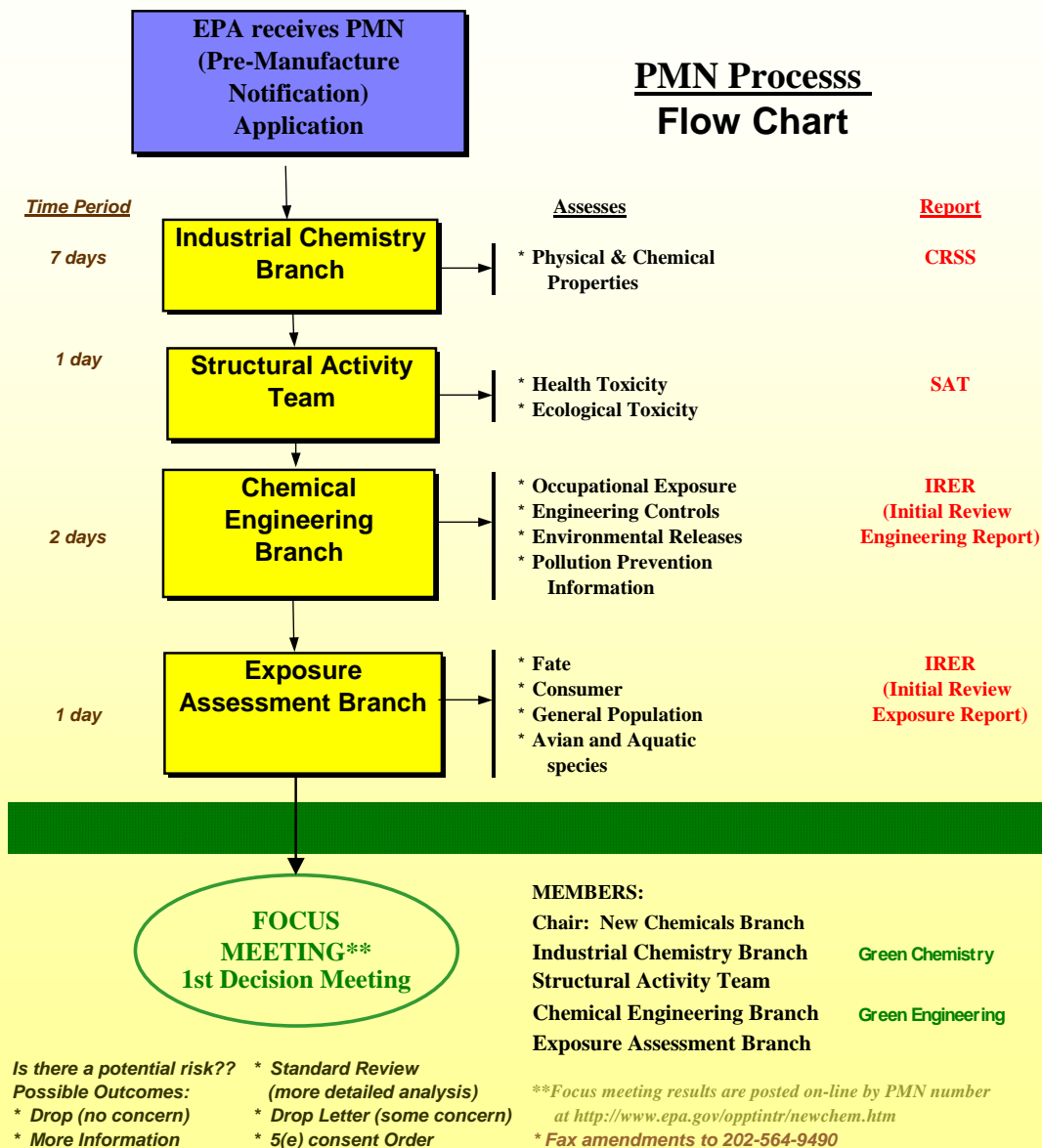
- **ChemSTEER – Material Flow - Metrics**

- Estimates exposure and release activities associated with the manufacture, processing, or use of the chemicals
- Provides quantitative results for worker exposure via inhalational and dermal contact
- Provides estimates for releases to all environmental media



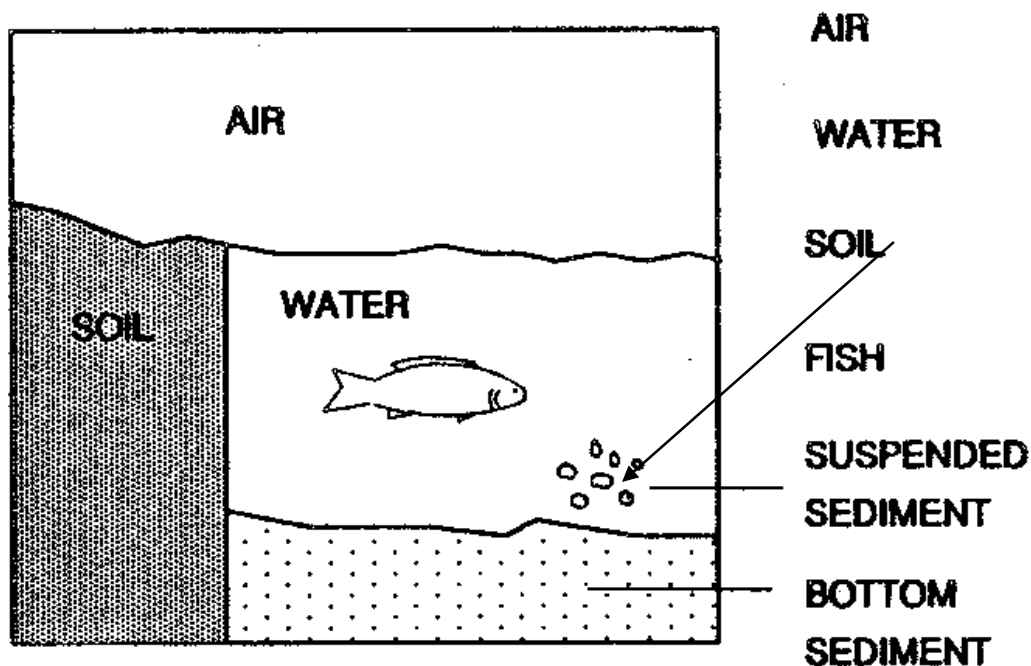
<http://www.epa.gov/oppt/exposure/pubs/chemsteer.htm>

PMN Process Flow Chart



Can You Eat the Fish?

EPI Suite helps to answer that question!



Water Compartment Only

1 kg Hexachlorobenzene (Hx)

10^5 m^3 volume of water

10^{-3} kg organic carbon / m^3 water

0.1 kg fish / 100 m^3 water

**Molecular
Level**

Human Exposure : Fish Ingestion

0.5 kg of fish consumed

Dose due to ingestion?

Concentration in the Fish (mg/kg)?

**Public
Domain**

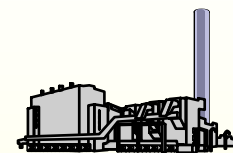


Operations Modeled in ChemSTEER

PMN Submitter Responsible for all Exposure and Releases

Chemical not
created yet
→
*Not available for
exposure/release*

Manufacturing
"creation of chemical"

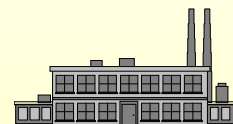


Raw Material
Manufacture

→
"Product" Out

"Raw Material" In
→

Processing
*"activity of
transformation"*



Intermediate Products

→
"Product" Out

"Raw Material" In
→

Use
*"destruction
of chemical"*



Final Product

→
Chemical Destroyed
*No longer available
for exposure/release*

Public Domain



Material Flow – Media of Release and Exposure Routes

OPERATION(S):

Workplace / workplaces with same/similar operations such that estimates of releases and exposures can be assumed to be the same.

Media of Release

Water

Air

Landfill

Incineration

Exposure Routes

Inhalation

Dermal

Drinking water

Inputs

MW

Vapor Pressure

Solubility

KG material

SAT/Model

ECO (EpiSuite)

Health (SARs)



Manufacturing

(PMN chemical is created or formed)

Production Volume?

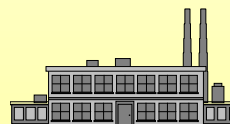
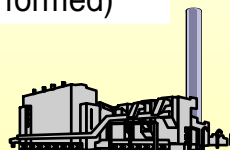
of sites?

Batch size?

Batches/Year?

Wt fraction?

of workers?



Site(s) typically controlled by the submitter
minimal in number (1 - 3), lower # of workers
larger, single point releases

Example Release(s) →

* equipment cleaning

* sampling

Exposure Activities(s) →

* loading into transport containers

* sampling

**Public
Domain**

Contact Information

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Promoting Environmental Stewardship through Industry/Government Collaborative Partnerships

Carlos Ramos
EPA Region 2

November 18, 2008



Region 2 Pollution Prevention Office

- Promotes P2 approaches by providing:
 - Direct technical assistance
 - Economic assistance
 - States
 - Local governments
 - Nonprofits
 - Academia
 - Outreach and education
 - Partnership Building



Activities To Date: Partnership Building

- Convene leading industry change agents and EPA National Technical Experts to share ideas related to green chemistry and green engineering innovations relevant to the pharmaceutical industry, better defining industry wide footprint, and initial stewardship opportunities.
- Bring together leading industry change agents with plant managers from manufacturing facilities in Puerto Rico to share insights, create case studies that can showcase the environmental and business opportunities for solvent reuse, recovery and third party exchanges.
- Bring in other critical stakeholders from within EPA and external to EPA, such as FDA that will encourage the successful implementation of proposed case studies.



Activities To Date: Outreach and Education

- September 27, 2007 Workshop – 70 Participants
- January 17, 2008 Video Conference – 40 Participants
- July 22, 2008 Video Conference – 29 Participants
- Develop, Update, and Maintain Web Page:
http://www.epa.gov/region02/p2/p2_catalog_of_activities.html



Activities To Date: Financial Assistance

- Identify as a priority green chemistry and engineering for our P2 and Source Reduction Assistance Agreement Grants.
- Target Assistance Agreement resources to Academic leaders and change agents – Rowen University
- Exploit other regional discretionary financial resources for continued outreach and education.



Activities To Date: Direct Technical Assistance

- Facilitate industry access to EPA's national expertise and other academic and private expertise
- Connect our regional local site-specific technical expertise through the Caribbean Environmental Protection Division with national expertise and other academic and private expertise.
- Initiate an industry partnership – EPA Pilot Compact in Puerto Rico.



Pharmaceutical Stewardship in Puerto Rico

- Largest concentration of pharmaceutical companies in the world.
- Exports more pharmaceutical products than any state in the U.S.
- Pharmaceutical industry is a large contributor to Puerto Rico economy
- Stewardship opportunity: solvent recovery
- Stewardship pilot project with EPA



Puerto Rico Stewardship Opportunities

- No solvent export off the island
- Recovery/reuse of insoluble solvents (e.g., dichloromethane, toluene)
- Resale of soluble solvents (e.g., methanol)
 1. Electronics /Semiconductor
 2. Electroplating/Rubber/Varnish
 3. Machinery Manufacturing and Repair



Pharmaceutical Stewardship Pilot Project

- 8 Puerto Rico facilities participating
- Facilities: Examine solvent usage, recovery, and resale opportunities; set reduction targets; implement activities; provide results data to EPA
- PRMA: Coordinates with local, state and federal agencies and supports facility efforts
- Model developers: Assist in quantifying opportunities and results
- EPA: Provides information (e.g., impact of new RCRA rules); technology transfer; and awards and recognition



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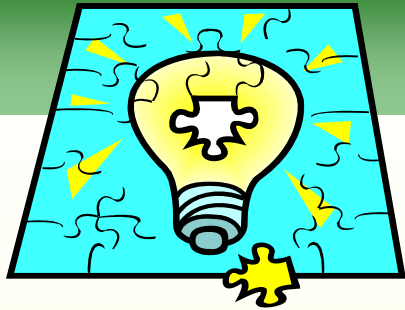


Recap: Putting the Pieces Together

**Sharon Austin,
EPA Green Engineering Program**

November 18, 2008



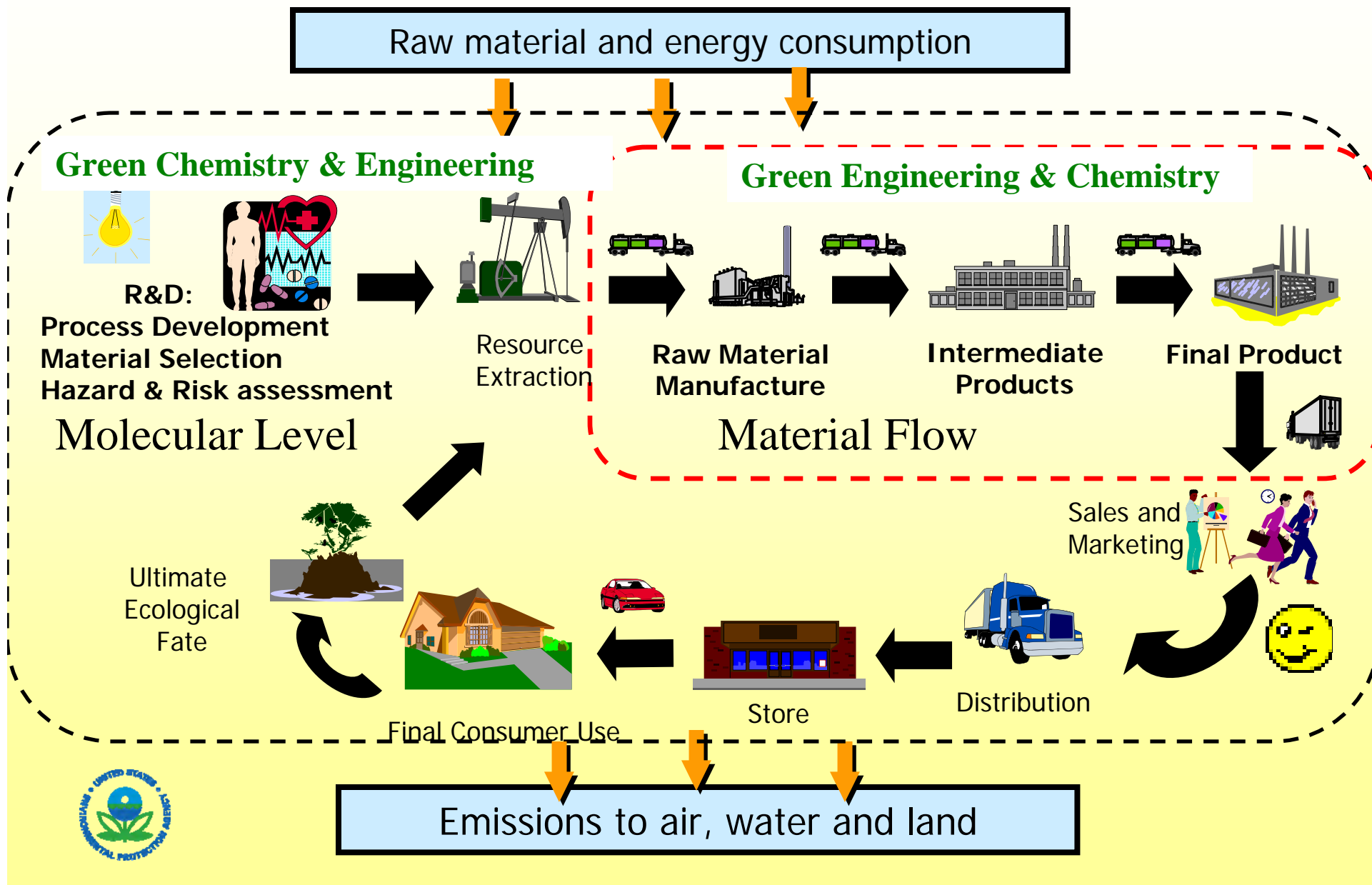


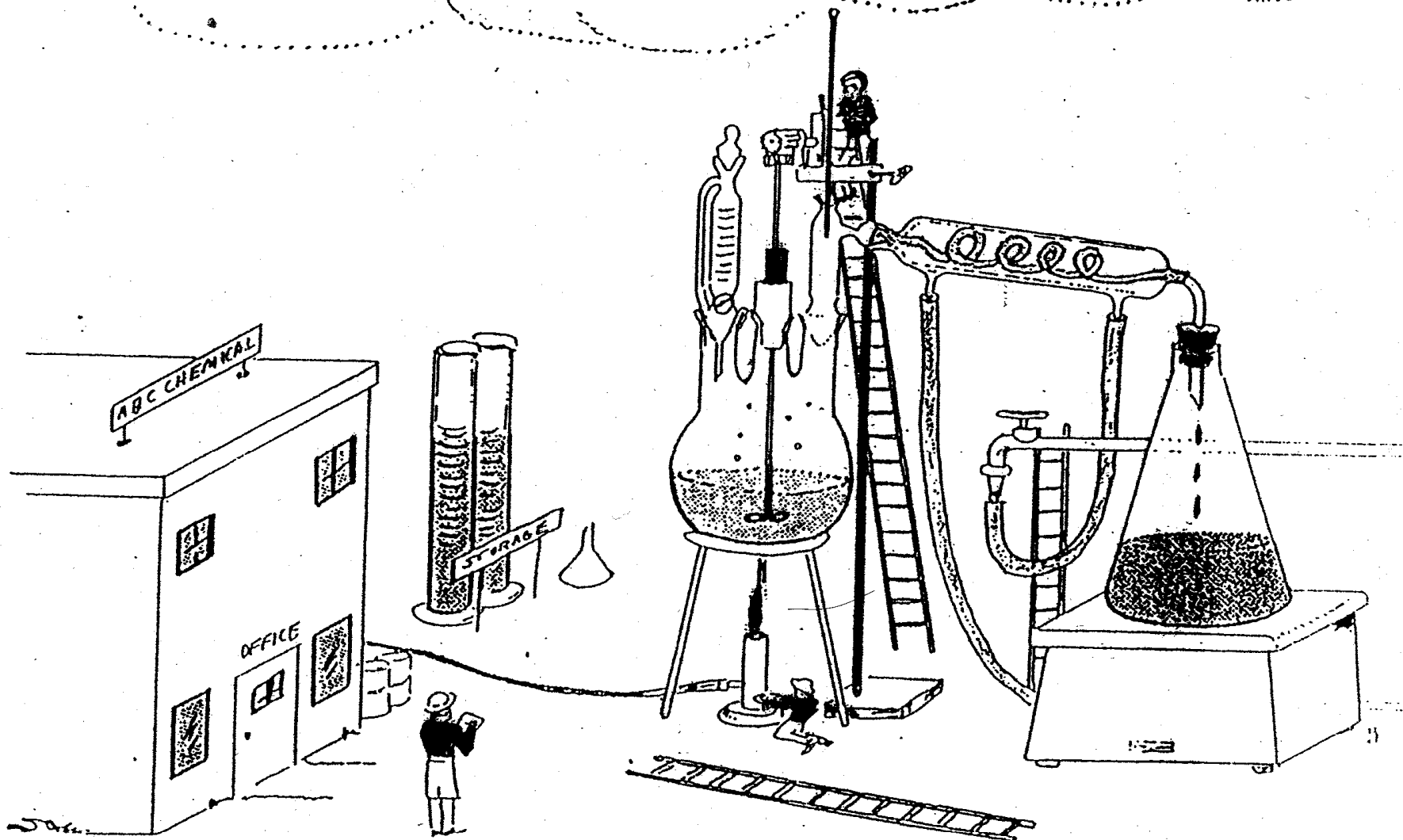
Putting the Pieces Together

- Best option: use of ideal solvents
- Take advantage of free tools
- Regional activities:
 - Target sectors, bundling of programs (Region 3)
 - Pilot project, identify opportunities (Region 2)
- Case studies/tech transfer
- Material flow to metrics (GHGs, \$ savings)



The Very Big Picture a Little Closer





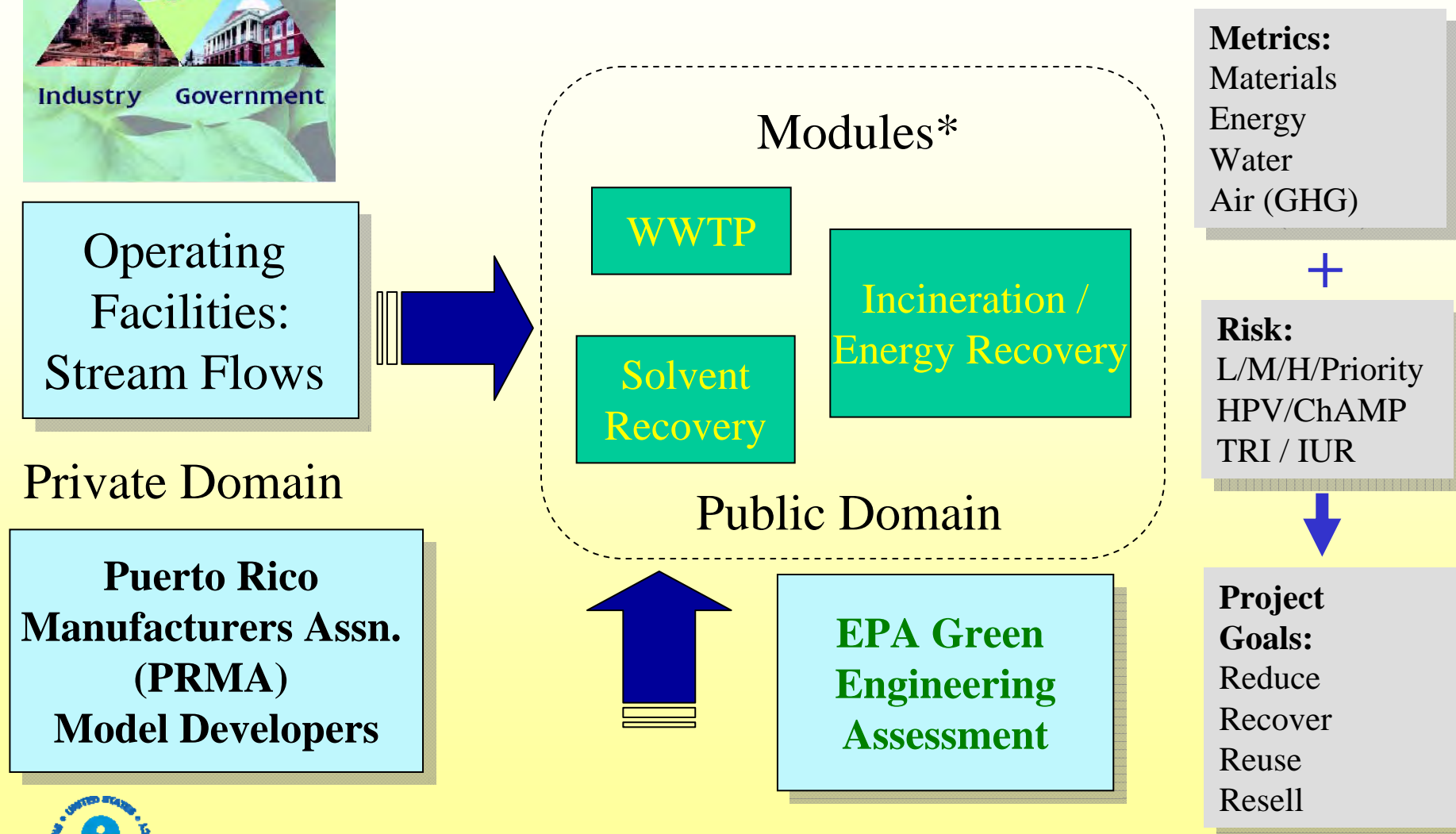
THE BENCH SCALE RESULTS WERE SO GOOD WE BYPASSED THE PILOT PLANT

Academia



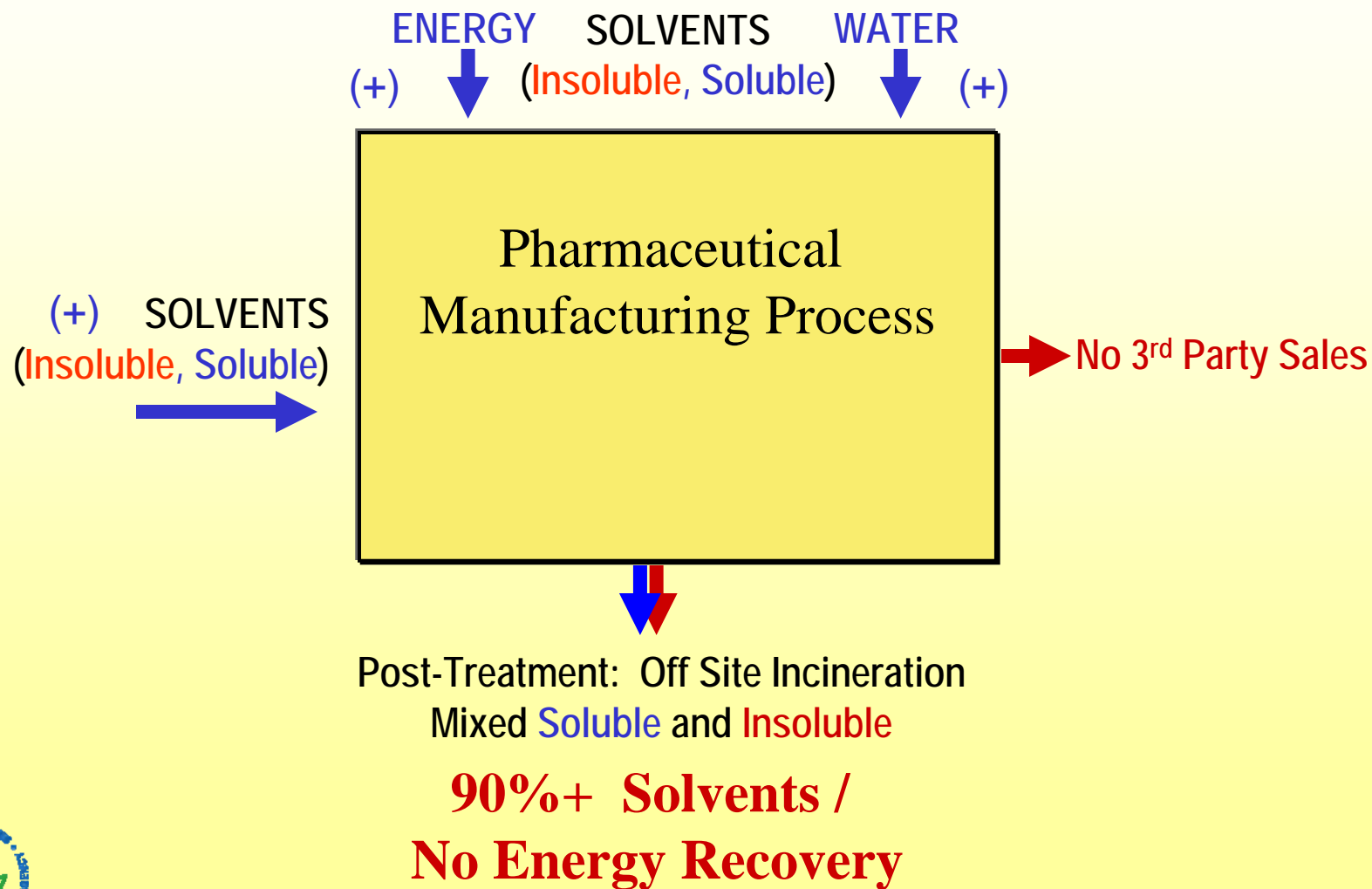
Industry Government

Material Flow to Metrics



*Jimenez-Gonzalez C, Overcash MR and Curzons AD. J. Chem. Technol. Biotechnol. 71:707-716 (2001)

Current Scenario – Handling as Waste



Environmental Impact of Solvent Management

2006 TRI Releases

- 122 million pounds of spent solvents **incinerated off site** in 2006
- 50% of the releases are soluble (50% solvent, 50% water), with methanol being the top solvent
- 50% of releases are insoluble, with dichloromethane being the top solvent



Environmental Impact of **Off Site Incineration**

- **Energy:** 90 trillion BTUs
- **GHGs:** 140,000 metric tons
- **VOCs, SO_x, NO_x:** 1.5 million pounds
- **Water:** 4 million gallons
- No energy recovery
- Loss of materials



Green Engineering Opportunities: Solvents

Solvent Selection, Recovery and Reuse

- Solvent selection guides already developed by industry and academia
- 99 kg waste/1 kg API - recovery has diminishing returns due to limitations on Capital Equipment, all utilized in manufacturing intermediates / API
- Ideal is a palette of solvents geared towards the chemistry you have to run and continuously recycle, purify and replenish (10% bottoms) as needed

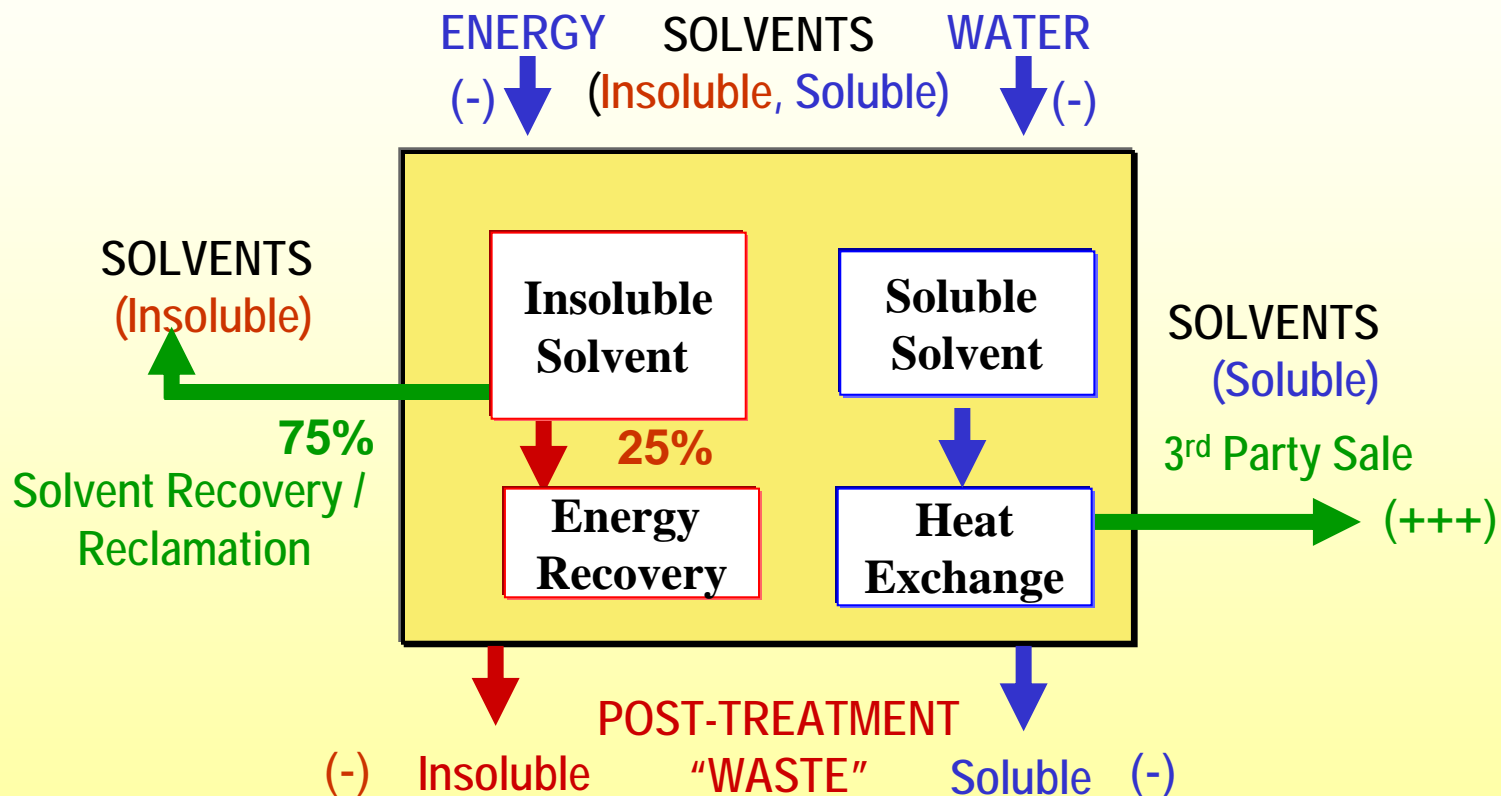
“We pay for the solvent, we pay for the capital to manage it, and we pay to burn it.”

The Materials & Energy that are invested in solvents make it a high (\$\$) value material!

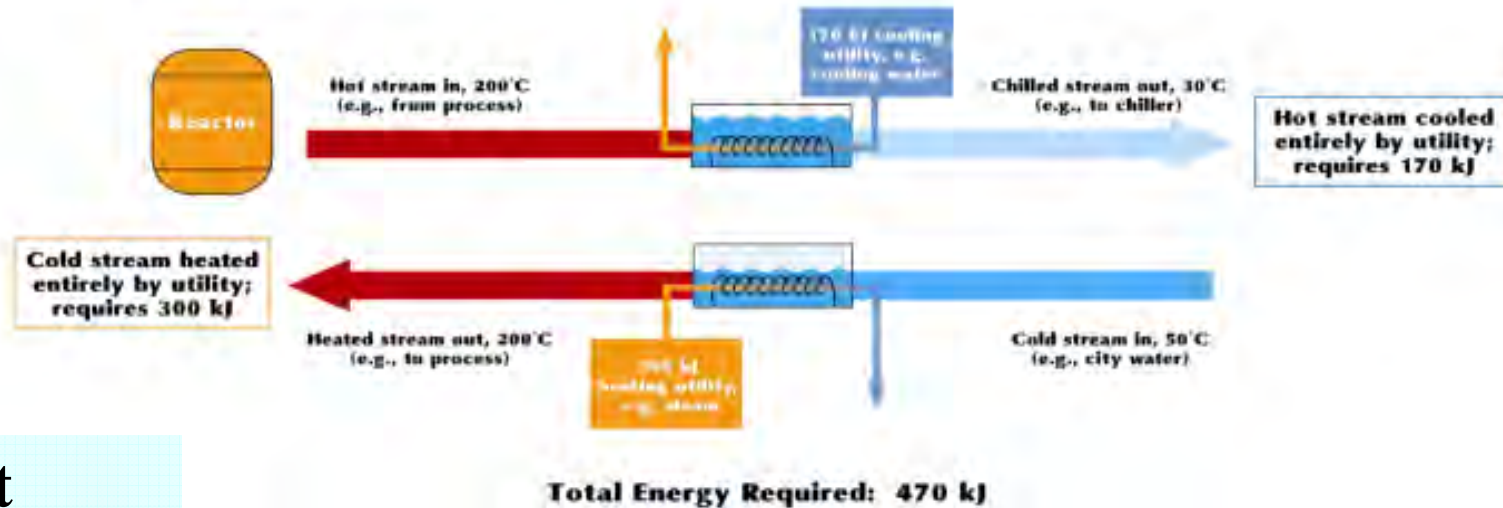


Adapted from / Courtesy of: David J. C. Constable, GlaxoSmithKline

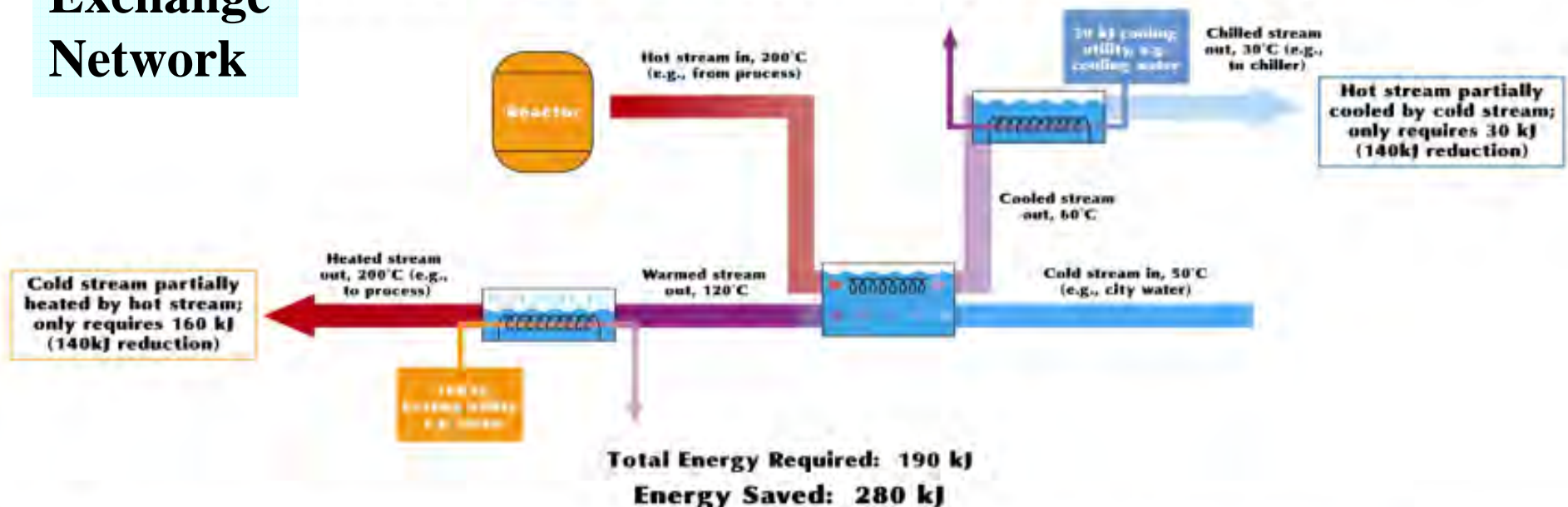
Green Scenario – Handling as Secondary Product



The cold stream begins at a temperature of 50 °C, and ends at a temperature of 200 °C. Similarly, the hot stream begins at a temperature of 200 °C and ends at a temperature of 30 °C.

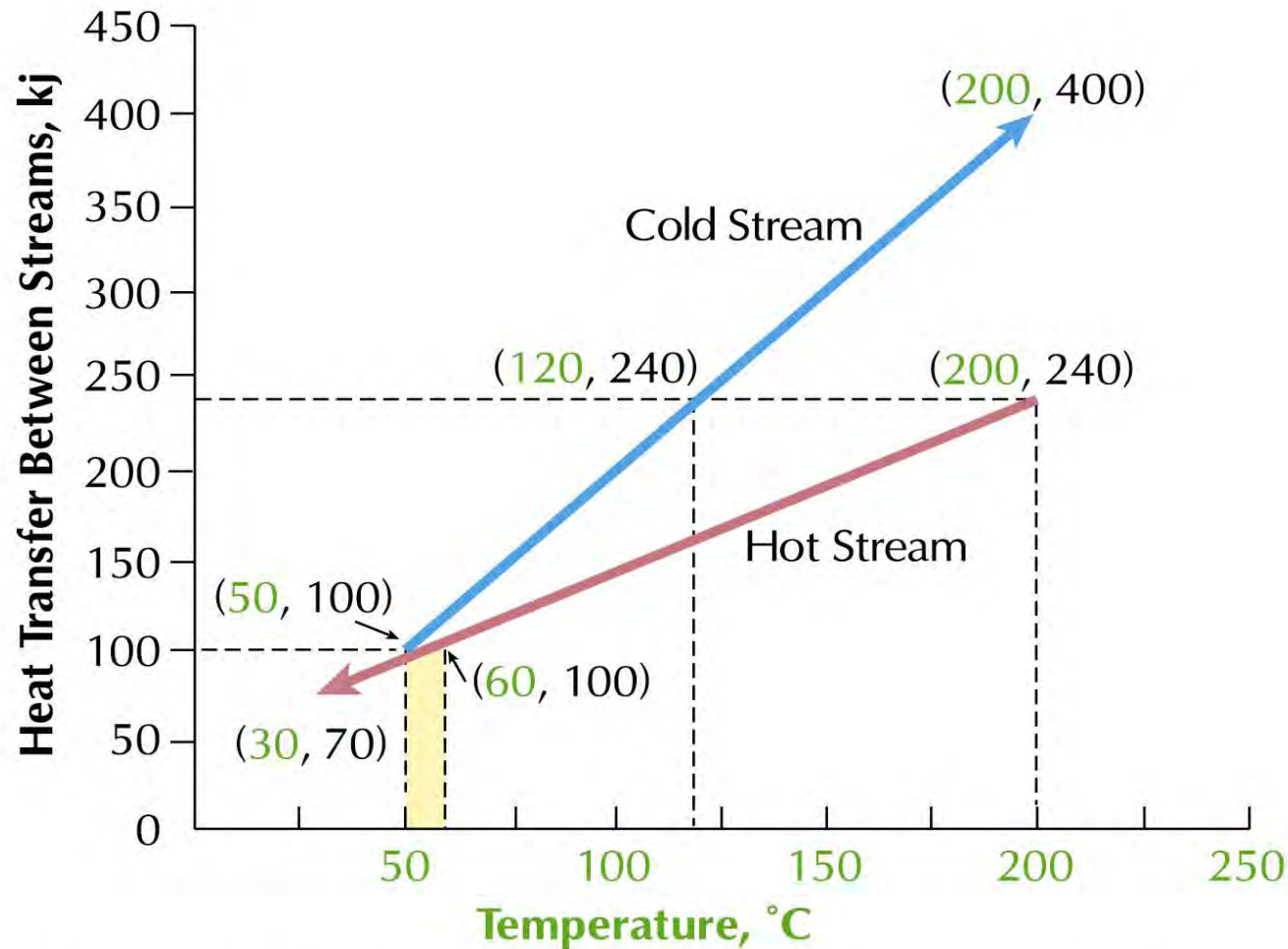


Heat Exchange Network



Under optimum heat transfer conditions, as shown in the pinch diagram at right, the cold stream is heated from 50 °C to 120 °C in the exchanger and the hot stream is cooled from 200 °C to 60 °C.

Heat Exchange Thermal Pinch



Hot stream and cold stream load line diagram for heat exchange network synthesis at an optimal temperature difference of 10°C (shaded region).

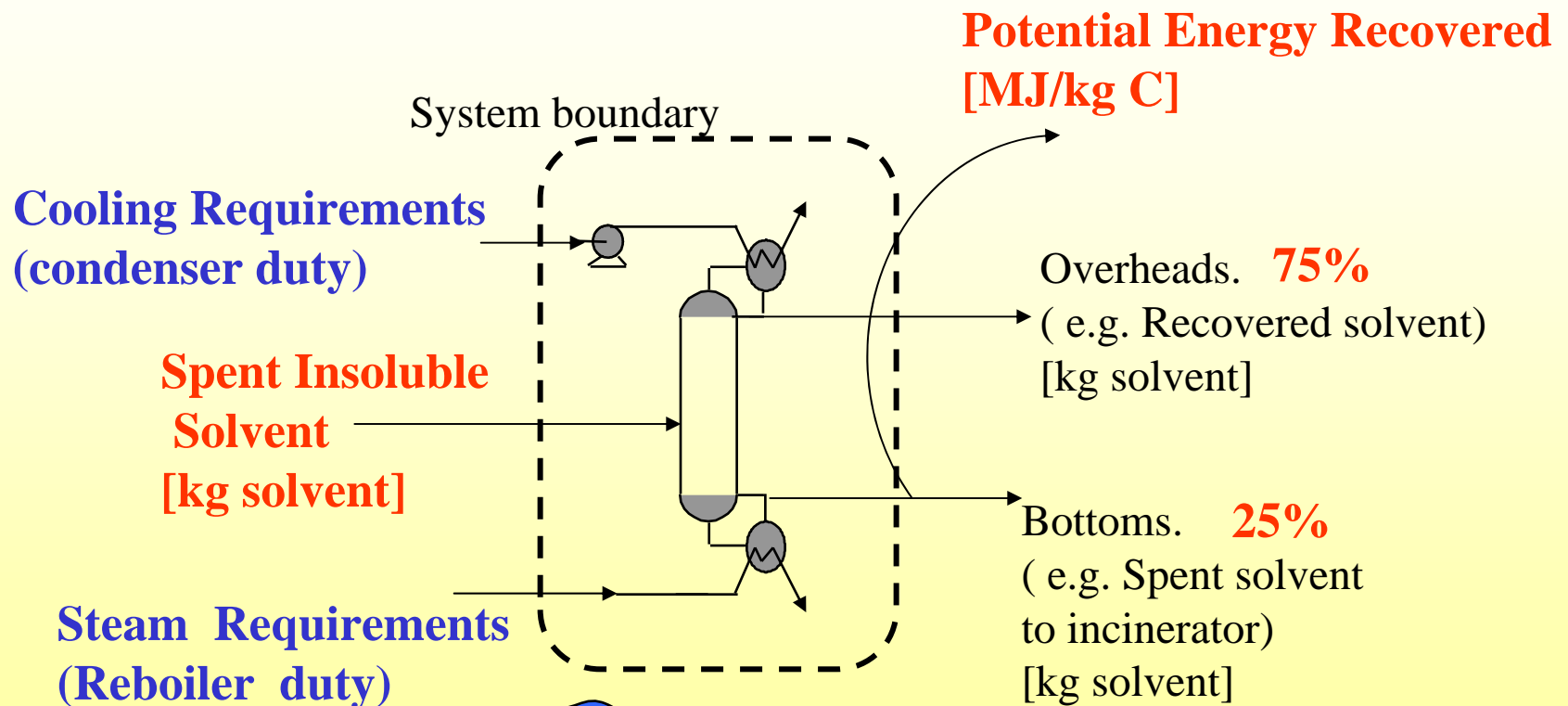
Heat Integration and Waste Water Recycle Case Study

Using Dowtherm A, the reactor cooling water stream, the feed to the reactor is heated to 225 °C, and Dowtherm A is cooled to 160 °C. Reduction in the amount of high pressure steam on the order of 3316 kg/h.

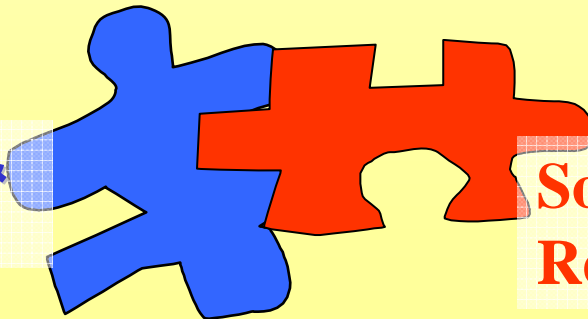
The source of heat for production of low pressure steam was changed to the remaining heat in the Dowtherm A cooling loop. This reduced the amount of high pressure steam needed by 15959 kg/h.



Solvent Recovery Module



HEN & MEN



Solvent & Energy Recovery



Methanol Institute
Voice of the Global Methanol Industry
www.methanol.org

"The Methanol Institute gives our industry a strong voice in the development of public policies that can have an enormous impact on the creation of new markets and the expansion of existing markets."

Today, methanol is one of the world's most widely distributed chemical commodities. As a basic building block for hundreds of chemical products, methanol is being used safely and effectively in everything from plastics and paints, to construction materials and windshield washer fluid.

Third Party Markets (scorecard.org): Order of Use / Purity Needs

Heat Transferring Agents (Secondary Coolants), ¹

Printed Circuit Board, Semiconductors, Laboratory Chemicals, ²

Electroplating, Rubber, Pesticides, Wood Stains & Varnishes, ³

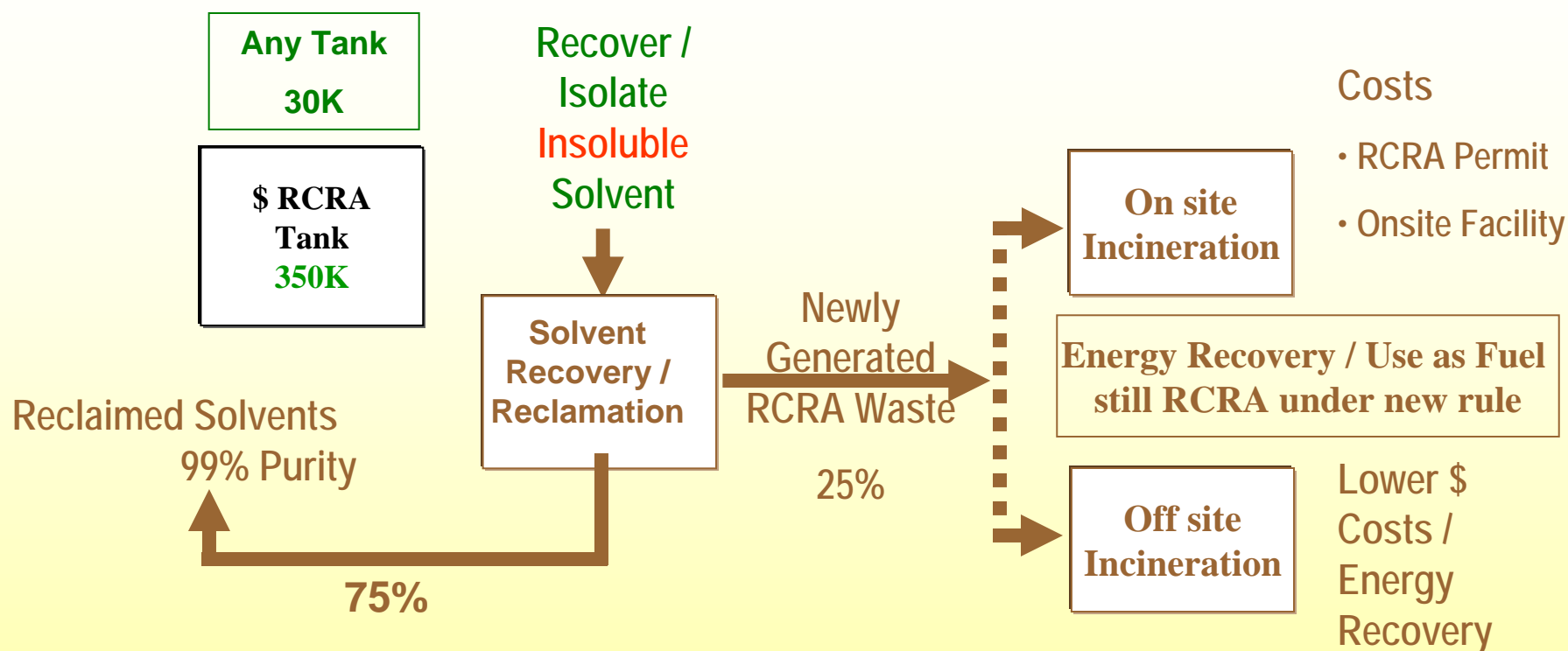
Machinery Mfg and Repair, Paint Mfg & Stripping, and Printing. ⁴

Revised Definition of Solid Waste Rule

- Original proposal published October 28, 2003
- Supplemental proposal published March 26, 2007 (72 FR 14172)
- Final rule signed October 7, 2008 (awaiting publication in the FR) (60 day implementation)
- <http://www.epa.gov/epawaste/hazard/dsw/rulemaking.htm>
- Applicability for solvent recycling



Insoluble: Dichloromethane/Toluene



\$ RCRA
Tank
90 day storage

Any Tank
1 year
storage

Legend

Current Hazardous Waste (RCRA) Rules

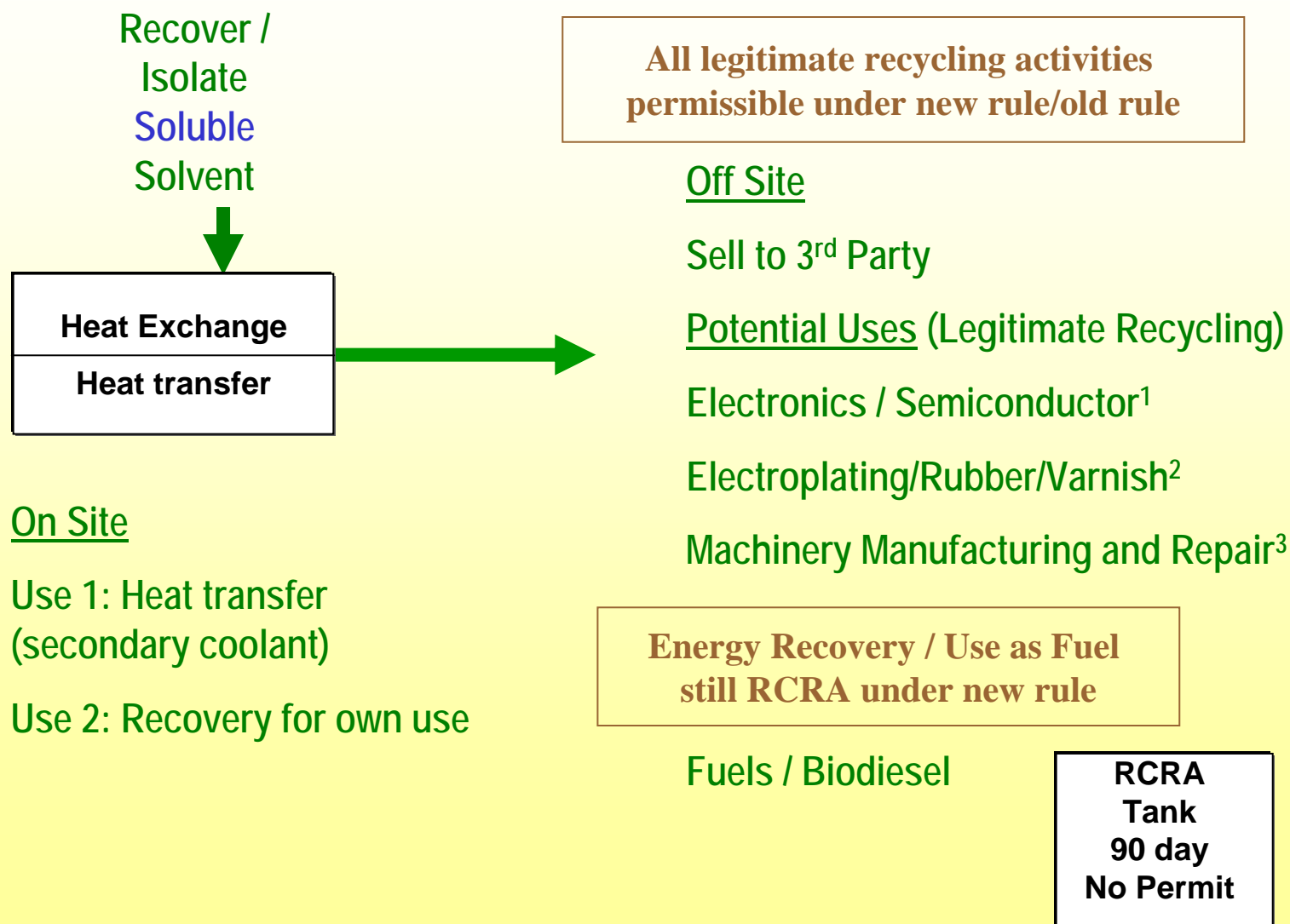
New RCRA Rules

Same Under New and Old RCRA Rules

RCRA: Resource Conservation
and Recovery Act



Soluble (H2O): Methanol



Greening Use of Solvents

Insoluble (Dichloromethane)

- High-risk carcinogen: Find alternatives (e.g., dipolar aprotic solvents, alkanes)
- Isolate and recover (75%) in closed systems

Insoluble (e.g., Toluene)

- Isolate and recover solvent (75%)
- Incinerate / energy recovery
- DO NOT sent to wastewater treatment*

Soluble (Methanol)

- Substitute with non-hazardous alternative (e.g., 1 or 2-butanol)
- Take advantage of water as heat sink: use in heat exchange
- Limit releases with leak detection and repair
- DO NOT incinerate
- Avoid / minimize sending to wastewater treatment*
- Recover solvent for resale (3rd party markets)



* *Primary energy use in wastewater treatment is for moving chemical and aeration*

Green Engineering Opportunities: Facility / Peripheral Systems

70% of all energy consumed is for steam and cooling

Energy Consumption



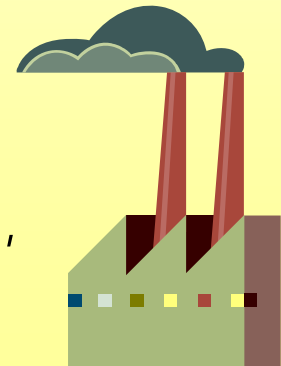
Process Emissions



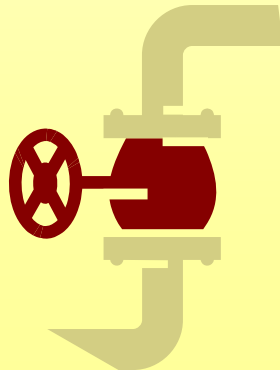
Cooling Water and
Steam Utilities



Process Wastes



Fugitive
Emissions



Emissions from Waste
Treatment (Incineration,
Wastewater Treatment,
Landfill, etc)

Green Engineering Opportunities: Utilities – Cooling / Once Through Water

- **Iron corroded off of piping produces doubles its own mass as iron oxide.**
- **This deposit – 10 tons equate to almost 100 cubic feet – can plug piping and impede water flow.**
- **Photo shows thinning of pipe wall and voluminous deposit.**



- Reduces heat transfer and raises electricity costs (increased pumping)
- Water treatment will prevent deposition and corrosion byproducts, especially when applied to heated streams
- Impede heat transfer in specific areas / thermal pockets



Optimization Projects and Procedures

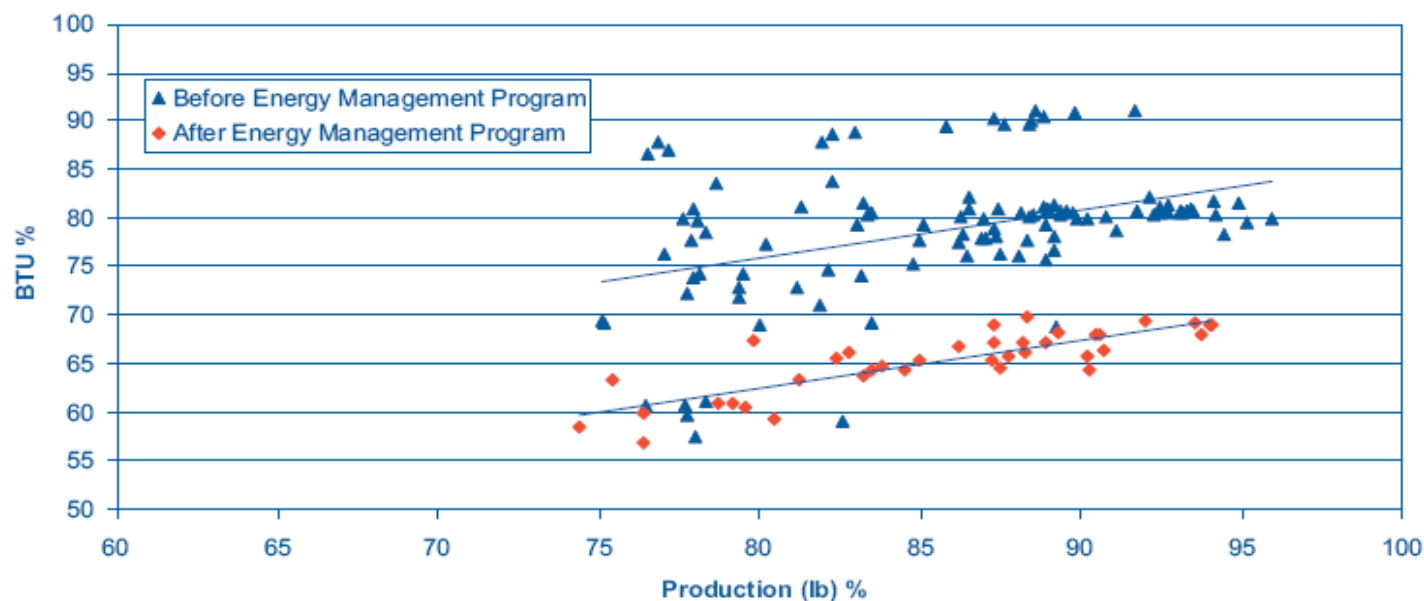
- A wide range of optimization projects and procedures can contribute to plant wide energy savings:
 - **Steam Generation:** Tighter combustion targets, CO controls, combustion analysis
 - **Steam Transmission:** Utility leak reporting and repair program, steam trap maintenance, condensate recovery
 - **Steam Consumption:** Re-evaluation of distillation targets and column sequencing, heat integration of condensate and low pressure steam, high-efficiency electrical motors
- Changes performed in the utility plant



Following example from Texas Industries of the Futures / Department of Energy: Texas Petrochemicals LP, Texas Petroleum Energy Management and Distillation Optimization Case Study, December 2006, <http://www.showcasetexas.org/showcases.html>

Energy Management and Distillation Optimization

Distillation Project Energy Efficiency Improvement (Btu/lb)



\$950,000/yr energy & 11,500 tons/yr CO2 savings

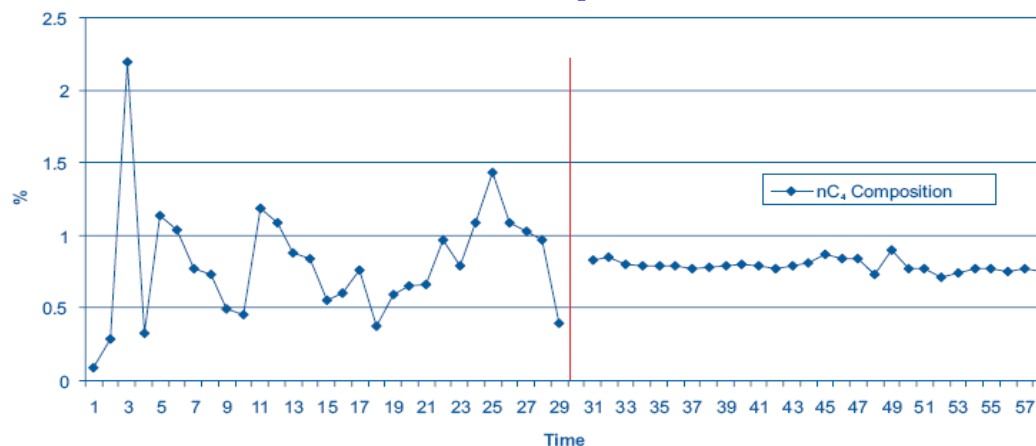
Pharmaceutical largest expenditure of energy is on steam



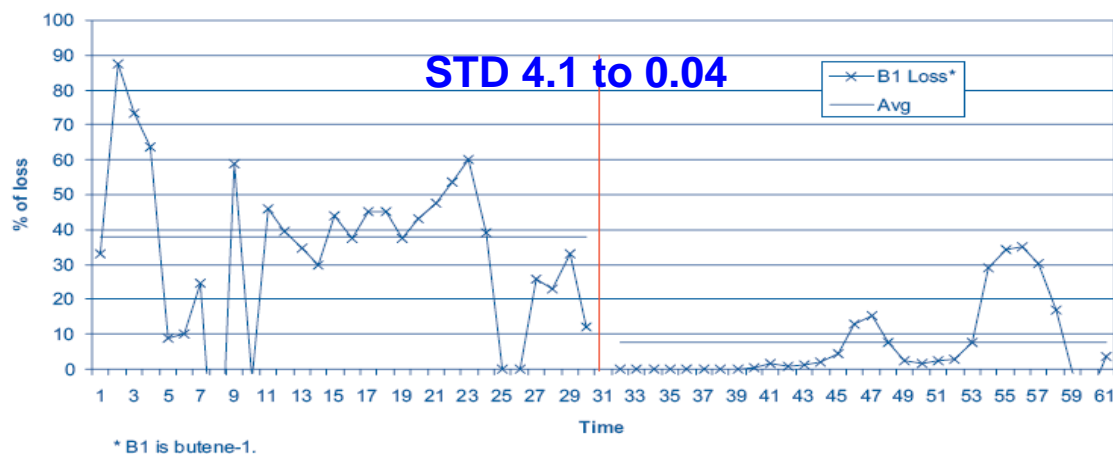
Energy Management and Distillation Optimization

Heat input to column controlled by composition control loop vs. bottoms level measurements

Overhead Composition Control



Product Loss Reduction



Pharmaceutical
Challenge:
Separation

Productivity
Benefit:

\$2.1 million/yr

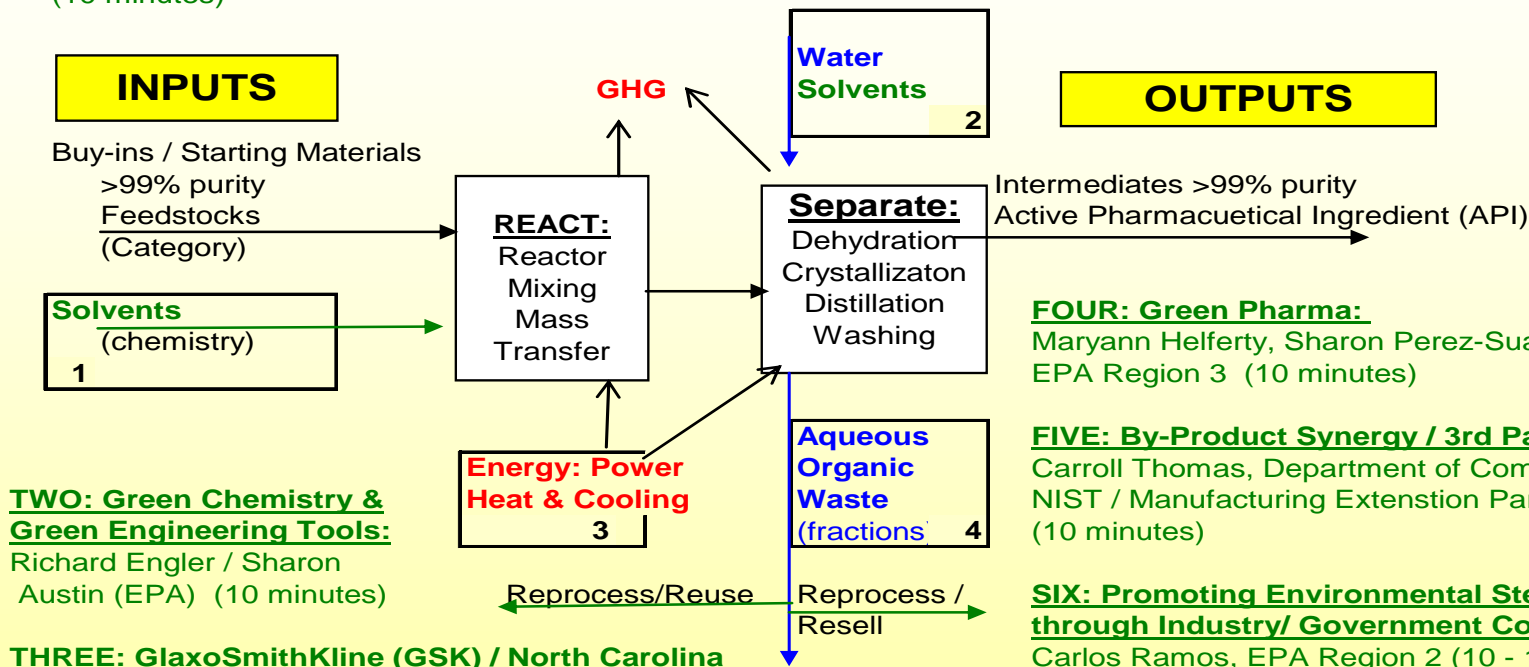
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Contact Information

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